PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference WRU 0255 PB	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/US2004/026787	International filing date *(day/month/year)* 18 August 2004 (18.08.2004)	Priority date *(day/month/year)* 18 August 2003 (18.08.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant WRIGHT STATE UNIVERSITY		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 21 February 2006 (21.02.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Beate Giffo-Schmitt
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Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

REC'D 14 MAR 2005
WIPO PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	10 MAR 2005
Applicant's or agent's file reference WRU 0255 PB	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US04/26787	18 August 2004 (18.08.2004)	18 August 2003 (18.08.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12N 15/86, 15/48, 15/49 and US Cl.: 435/456, 320.1

Applicant

WRIGHT STATE UNIVERSITY

1. This opinion contains indications relating to the following items:

- [X] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [X] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. 571 273-8300	Authorized officer Michael D. Burkhart Telephone No. 571 272-2915

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/26787

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/26787

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 6-7, 11-12, 16, 18, 21-25	YES
	Claims 1-5, 8-10, 13-15, 17, 19-20, 26	NO
Inventive step (IS)	Claims 6-7, 11-12, 16, 18, 21-25	YES
	Claims 1-5, 8-10, 13-15, 17, 19-20, 26	NO
Industrial applicability (IA)	Claims 1-26	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1-5, 8-10, 13-15, 17, 19-20, and 26 lack novelty under PCT Article 33(2) as being anticipated by Mansky et al (*J.* Virol., 2003). The claims are drawn to a lentivirus-based vector that comprises: at least a portion of a lentivirus genome; disrupted *gag*, *pol*, and *env* genes; a mutational cassette comprising a mutation target sequence and associated promoter and a selectable marker driven by an IRES. The vector may be transduction and infection competent and be based on any of the lentiviruses listed in claims 3-4. The selectable marker may be a positive selection and the mutation target may be greater than 700 base pairs. Also claimed is a cell comprising the vector, which may be dividing or nondividing, and a method to assay the mutation rate of retroviruses.

Mansky et al disclose an HIV-1 based vector lacking functional *gag*, *pol*, and *env* that comprises a *lacZ* mutation target linked to an SV40 promoter and a neomycin resistance selectable marker driven by an IRES (see Figure 1, A and B, and Materials and Methods, pg. 2072). The *E. Coli lacZ* gene is approximately 3 kilobases long. This defective provirus is transfected into COS-1 cells along with helper plasmids expressing functional *gag*, *pol*, and *env* to produce infectious (i.e. transducable) vector virus (see passages above). Mansky et al also disclose a method to assay the mutation frequency of this vector comprising the steps of the instant claims (i.e. claim 17), see Fig. 1 B and Experimental protocol for generating a single round of HIV-1 vector replication under Materials and Methods, pg. 2072.